Taking Femoropopliteal Excimer Laser Photoablation Therapy to the Next Level: Defining the Role of the TURBO-Booster Guiding Catheter in the CELLO Registry

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Excimer laser has been shown to be an effective and safe photoablative tool in treating infrarenal atherosclerotic obstructive disease. Excimer laser is highly clinically effective in treating infrapopliteal disease in patients with critical limb ischemia and in promoting limb salvage. Because of the smaller channel created by the TURBO-Elite laser catheter, optimally treating femoropopliteal vessels with the laser alone has been limited. The TURBO-Booster laser guide catheter was invented to overcome this limitation by creating off-axis photoablation, thus widening the lumen obtained with the excimer laser in femoropopliteal vessels.

In the pivotal CliRpath Excimer Laser System to Enlarge Lumen Openings (CELLO) multicenter registry, the TURBO-Booster laser guide catheter with the TURBO-Elite laser catheter was tested for safety and effectiveness in de novo femoropopliteal lesions in patients with claudication. The primary end-point was the reduction in index lesion percent diameter stenosis following immediate laser ablation and before any adjunctive treatment. Adjunctive balloon angioplasty was performed in 64.6%, angioplasty + stenting in 23.1%, and laser only in 12.3% of cases. Diameter stenosis was reduced to 34.7% ± 17.8% (meeting the primary endpoint of the study) with the laser only and to 21% ± 14.5% after adjunctive treatment; 98.5% of lesions met the primary endpoint with at least a 20% reduction in diameter stenosis. The intermediate-term follow-up showed that patency (<50% diameter stenosis) was 59% at 6 months and 54% at 1 year. TLR was required in 23.1% of CELLO participants at 1 year. Walking impairment and functional status assessments were improved at 1 month after treatment, with persistent improvement at 12 months. There were no safety issues related to the device.

Several important observations need to be emphasized in this well designed multicenter prospective registry. First, using core laboratory–monitored intravascular ultrasound (IVUS) and angiographic analyses, CELLO clearly demonstrated that the TURBO-Booster is an important adjunct to the TURBO-Elite laser catheter for achieving excellent acute angiographic results with no compromise to safety. Approved by the Food and Drug Administration based on the CELLO data and now widely available, the TURBO-Booster has recently evolved into the new generation Turbo-Tandem, in which the 7-F laser guide catheter has been combined with a 2.0-mm excimer laser catheter to make the device more user-friendly and eliminate the need for the operator to assemble the 2 catheters. Even with the current design of the TURBO-Booster guiding catheter, training operators on its use appears to be a relatively easy task. In CELLO, one training case per principal operator was required prior to enrollment.
These “training cases” had the same outcome at 1 year as the post training procedures. In a busy laboratory it is more likely that operators widely will adopt easy-to-learn tools and techniques rather than complex ones to minimize procedure length, radiation exposure, and contrast use, as well as to ensure continued patient safety.

Second, in CELLO, the lesions were relatively short in length (5.6±4.7 mm); without randomization against balloon angioplasty, it is unclear whether the acute angiographic results are superior to balloon angioplasty alone. However, 62% of these lesions were moderately to heavily calcified, as judged by the angiographic core laboratory, and 20% were total occlusions; both these variables are predictors of suboptimal results and the need for stenting.\(^3\) Despite this, the stenting rate was limited to only 23% of patients (8 grade C or higher dissections, 6 suboptimal residual stenoses, and 1 threatened acute closure). This stent rate, which is lower compared to similar historic lesions treated with balloon angioplasty alone,\(^4,5\) is a clear advantage that seems to be related to laser debulking, which may improve vessel compliance and reduce the incidence and/or extent of dissection.

Debulking in general is associated with a reduced stent utilization and improved vessel compliance, which are advantageous in treating femoropopliteal and tibial lesions.\(^5\) Stenting of the femoropopliteal segments with bare nitinol stents has inherent disadvantages.\(^6,7\) With the advent of localized antiproliferative drug delivery,\(^8\) therapies that lead to acute optimal angiographic results without primary stenting may likely become an initial preferred strategy. As previously discussed,\(^9\) achieving optimal acute angiographic results without primary stenting may likely become an initial preferred strategy. As previously discussed,\(^9\) achieving optimal acute angiographic results without primary stenting and using adjunctive antiproliferative therapy and embolization protection for the tibial vessels may likely form an optimal strategy effective in treating infrainguinal obstructive peripheral arterial disease. Laser therapy may pave the way for such a strategy, as good angiographic results can be achieved with less dissection and stenting using the TURBO-Booster catheter and with limited distal embolization, as seen in the DEEP EMBOLI study.\(^10\) In the latter study, distal embolization with the laser was comparable to angioplasty and stenting, but the rate was substantially lower than reported for SilverHawk atherectomy.\(^11\) In the CELLO registry, clinically significant distal embolization was not reported or observed by the angiographic core laboratory.

Third, similar to other devices to treat de novo femoropopliteal lesions, intermediate and long-term primary patency remained a challenge. In CELLO, there was a decline in primary patency at 6 months (59.3%) and 1 year (54.3%) from 96.9% at 1 month based on duplex ultrasound criteria. When accounting for the 15 patients who underwent target lesion revascularization (TLR) and were excluded from the primary patency analysis at 1 year, overall angiographic- and duplex-documented primary patency was seen in only 25/61 (41%) patients (4 patients excluded). It should be noted, however, that a conservative peak systolic velocity ratio of <2.0 was used to determine patency, so the true patency rate may have been underestimated. Similarly, data from Scheinert et al.\(^12\) in patients with total occlusions treated with the excimer laser showed a primary patency rate of 33.6% at 1 year. Furthermore, Steinkamp and colleagues\(^13\) reported a primary patency rate of 49.2% in short superficial femoral artery occlusions (1–10 cm) treated with the excimer laser at a 36-month follow-up. Finally, Stoner et al.\(^14\) reported a primary patency rate of 44% at 461±49 days in 40 patients (47 femoropopliteal/infrapopliteal lesions) treated with laser atherectomy. These primary patency data appear to be comparable to balloon angioplasty\(^15,16\) and inferior to stenting,\(^4,17\) but this observation can be addressed conclusively only in randomized clinical trials.

CELLO, however, provided some insight into the mechanism of reduced patency with the laser at 1 year. The initial gain in the minimal luminal diameter was related equally to plaque debulking and vessel stretching as seen on IVUS. Loss of patency, which was not seen at 1 month, was apparent at 6 and 12 months, strongly suggesting that negative vessel remodeling and/or smooth muscle cell (SMC) proliferation were the predominant mechanisms in lost patency rather than acute recoil immediately post laser. Distinguishing be-
tween SMC proliferation and negative remodeling is not clear in the CELLO trial since angiography and IVUS were not repeated at 1 year in these patients. The distinction between these 2 mechanisms, however, is important in designing future adjunctive antiproliferative therapies for use with the laser. If negative remodeling plays a dominant role in patency loss after laser therapy, then antiproliferative therapy added to laser treatment will likely be only partially effective in reducing restenosis. However, if SMC proliferation is the predominant mechanism of post-laser restenosis, then an adjunctive antiproliferative therapy will likely be highly effective in maintaining long-term patency.

Finally, even though patency was reduced at 6 months and 1 year, freedom from TLR for non-stented CELLO patients was 74%, which appears to be higher than the 46.2% freedom from TLR of non-stented balloon angioplasty patients in the Resilient trial but possibly lower than stenting (83.2%). Again, comparative randomized data are needed to determine how long-term TLR is affected by laser versus stenting. This apparent dichotomy between lower vessel patency and freedom from TLR, however, points to the importance of avoiding retreatment by relying on patency data alone in follow-up. Symptom-driven TLR coupled with objective testing may be a better approach to justify repeat revascularization in these patients.

In conclusion, the CELLO trial is a pivotal study that showed the safety and effectiveness of the TURBO-Booster guiding catheter when coupled with the TURBO-Elite laser catheter. Plaque debulking is enhanced, with a low stenting rate possibly due to improved vessel compliance and reduced dissection. CELLO also showed that acute recoil is less likely to contribute to a reduced patency rate at 6 and 12 months. Whether reduced patency is related to SMC proliferation or negative remodeling, or both, remains to be answered. Also, we do not know if this aggressive debulking strategy with the TURBO-booster is superior to a less aggressive debulking therapy or plaque modification therapy with the TURBO-elite excimer laser alone. Randomized studies testing those strategies are also needed.

REFERENCES


